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09/780,717	02/09/2001	Timothy G. Helentjaris	35718/208677 (5718-126)	6907

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EXAMINER
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KALLIS, RUSSELL

ART UNIT	PAPER NUMBER
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1638

DATE MAILED: 10/23/2002

11

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/780,717

Applicant(s)

HELENTJARIS ET AL.

Examiner

Russell Kallis

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-22 is/are pending in the application.
- 4a) Of the above claim(s) 1 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 2-22 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

## Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 5,6,7,8.

- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_

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## DETAILED ACTION

### *Election/Restrictions*

Applicant's election without traverse of Group II and SEQ ID NO: 1 encoding SEQ ID NO: 2 in Paper No. 10 is acknowledged.

### *Claim Rejections - 35 USC § 112*

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 2-22 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant broadly claims a nucleotide sequence encoding a maize invertase inhibitor of SEQ ID NO: 1, a nucleotide sequence having 80% sequence identity to a nucleotide sequence encoding a maize invertase inhibitor of SEQ ID NO: 1, a nucleotide sequence that corresponds to an antisense sequence of a nucleotide sequence encoding a maize invertase inhibitor of SEQ ID NO: 1, a nucleotide sequence encoding a yeast invertase, and a nucleotide sequence that hybridizes under conditions of unspecified stringency to any one of the above nucleotide sequences or complementary sequences thereof.

Applicant describes a nucleotide sequence of SEQ ID NO: 1 encoding a maize invertase inhibitor of SEQ ID NO: 2, the antisense sequence of SEQ ID NO: 1 and a nucleotide sequence encoding a yeast invertase enzyme.

Applicant does not describe a nucleotide sequence having at least 80% sequence identity to a nucleotide sequence encoding a maize invertase inhibitor other than the nucleotide sequence of SEQ ID NO: 1, or sequences that hybridize under conditions of unspecified stringency to a nucleotide sequence encoding a maize invertase inhibitor of SEQ ID NO: 1, a nucleotide sequence having 80% sequence identity to a nucleotide sequence encoding a maize invertase inhibitor of SEQ ID NO: 1, a nucleotide sequence that corresponds to an antisense sequence of a nucleotide sequence encoding a maize invertase inhibitor of SEQ ID NO: 1, a nucleotide sequence encoding a yeast invertase, and complementary sequences thereof.

Given the claim breadth and lack of guidance as discussed above, the specification does not provide an adequate written description of the claimed invention.

See *University of California V. Eli Lilly and Co.*, 43 USPQ2d 1398 (Fed. Cir. 1997), which teaches that the disclosure of a process for obtaining cDNA from a particular organism and the description of the encoded protein fail to provide an adequate written description of the actual cDNA from that organism which would encode the protein from that organism, despite the disclosure of a cDNA encoding that protein from another organism.

The court also addressed the manner by which genus of cDNAs might be described: "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a

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recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." *Id.* At 1406.

3. Claims 2-22 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicant claims a method of modulating invertase activity and increasing yield in a dicot or monocot plant transformed with a nucleotide sequence encoding a maize invertase inhibitor, a nucleotide sequence having 80% sequence identity to a nucleotide sequence encoding a maize invertase inhibitor, a nucleotide sequence that corresponds to an antisense sequence of a nucleotide sequence encoding a maize invertase inhibitor, a nucleotide sequence encoding a yeast invertase, and a nucleotide sequence that hybridizes under conditions of unspecified stringency to any one of the above nucleotide sequences or complementary sequences thereof.

Applicant teaches a recombinant invertase inhibitor which inhibits maize invertase activity (Figure 1, page 2 lines 29-30 and page 3 lines 1-2), PCR detection of maize invertase inhibitor expression in leaf (Figure 2, page 3 lines 3-6), transgenic construct comprising the maize invertase inhibitor coding sequence (Figure 3, page 3 lines 7-9), overexpression of maize invertase inhibitor in leaf tissue of stable transgenic lines (Figure 4, page 3 lines 10-12), methods for transformation and regeneration of maize using a DNA construct containing the antisense sequence corresponding to SEQ ID NO: 1 using a particle bombardment method (Example 1), using an *Agrobacterium* mediated transformation method (Example 2), and transformation of soybean seedling by bombardment with 'the invertase inhibitor gene' (Example 3 page 28 lines

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15-16 and 28-31) and generation of transformation material by somatic embryogenesis in liquid media (Example 3, lines 17-27).

Applicant does not teach modulation of invertase activity and/or an increase in yield in any transformed plant using a DNA construct containing either an antisense or sense sequence of SEQ ID NO: 1, (a plant invertase inhibitor), or a nucleotide sequence encoding a yeast invertase. In addition, Applicant does not teach the isolation of any sequence with as low as 80% similarity to SEQ IDNO: 1, or sequence which hybridizes under low or moderate stringency thereto, or any plants transformed therewith.

An important consideration in altering or modulating the gene expression of a plant would be to take into account the unpredictable nature of transformation when several structurally related isoforms of a particular transgene maintain distinct mechanisms and modes of regulation. Vacuolar and cell wall invertases showed different responses to invertase which inhibitors due to substrate protection by sucrose of cell wall invertase but not vacuolar invertase suggests that the two invertases are regulated differentially by invertase inhibitors with respect to sucrose concentration (Sander A. *et al.*, FEBS Letters 385, 1996 pp.171-175; on page 174 column 2 lines 18-27).

This indeterminate nature is also evident at the whole plant level where attempts to modulate invertase expression had a deleterious effect upon plant growth due to photoinhibition and showed no benefit whatsoever with respect to growth or yield. Overexpression of invertase in transgenic *Arabidopsis* showed slight growth inhibition evidenced by the presence of anthocyanins and in transformed tobacco overexpressing invertase yielded plants stunted in their growth with bleached and necrotic areas developing on older leaves (Schaeven A. *et al.*, The

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EMBO Journal 1990, vol. 9, no. 10, pp.3033-3044; on page 3033 Abstract and page 3041 column 2 lines 8-56).

Another example of unpredictability resulted from an attempt to modulate invertase activity in the transgenic legume *Vicia faba* using a yeast invertase gene which showed a negative impact upon yield with respect to the storage of both protein and starch (Weber H. *et al.*, The Plant Journal 1998, 16(2) pp. 163-172; on page 169 column 1 lines 26-32).

Generally speaking, given the possible and most likely presence of uncharacterized multiple isoforms of invertase enzymes, and invertase inhibitors as well, expressed in various tissue types of a plant through the developmental phases of growth, especially during storage of starch; and given the polyploidic nature of many dicot and monocot crop plants; transformation with a single isoform of a polynucleotide encoding an invertase inhibitor or an invertase is a highly unpredictable factor to consider in any attempt to modulate gene expression and/or yield.

Given the lack of guidance, the absence of working examples in the specification, the breadth of the claims, and the unpredictability in the art, undue trial and error experimentation would have been required by one skilled in the art to transform and regenerate non-exemplified monocot and dicot plants with sense or antisense plant invertase inhibitor constructs or constructs comprising the polynucleotide encoding a yeast invertase and evaluate a multitude of non-exemplified regenerated plants with modulated invertase activity and/or increased yield. Undue experimentation would have also been required to isolate a multitude of non-exemplified invertase sequences with at least 80% sequence identity to SEQ ID NO: 1, or a multitude of sequences which hybridize under low or moderate stringency thereto, and to evaluate their ability

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to either encode a protein with invertase inhibitor activity or to modulate invertase activity and/or to increase yield in transformed plants.

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Dependent claims are included in all rejections.

At Claim 2, line 6, "a nucleotide sequence that corresponds to an antisense sequence" is indefinite. It is unclear if a nucleotide sequence that corresponds to an antisense sequence of another sequence is an exact match or not. It is also unclear whether the antisense sequence corresponds to the full length sense gene or only a portion thereof. Further "an antisense sequence" should read --the antisense sequence--.

At Claim 11, lines 11 and 15, "a nucleotide sequence that corresponds to an antisense sequence" is indefinite. It is unclear if a nucleotide sequence that corresponds to an antisense sequence of another sequence corresponds exactly or not. It is also unclear whether the antisense sequence corresponds to the full length sense gene or only a portion thereof. Further, "an antisense sequence" should read --the antisense sequence--.

At Claim 11, lines 15-16, "an antisense sequence for a plant invertase inhibitor", should read, --an antisense sequence of a sequence that encodes a plant invertase inhibitor--.

At Claim 14, lines 1-2, "an antisense sequence for a plant invertase inhibitor", should read, --an antisense sequence of a sequence that encodes a plant invertase inhibitor--.



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At Claim 15, lines 1-2, "the nucleotide sequence is a yeast invertase", should read, --the nucleotide sequence is a sequence encoding a yeast invertase inhibitor--.

At Claim 20, lines 11 and 15, "a nucleotide sequence that corresponds to an antisense sequence" is indefinite. It is unclear if a nucleotide sequence that corresponds to an antisense sequence of another sequence corresponds exactly or not. It is also unclear whether the antisense sequence corresponds to the full length sense gene or only a portion thereof. Further, "an antisense sequence" should read --the antisense sequence--.

At Claim 21, lines 11 and 15, "a nucleotide sequence that corresponds to an antisense sequence" is indefinite. It is unclear if a nucleotide sequence that corresponds to an antisense sequence of another sequence corresponds exactly or not. It is also unclear whether the antisense sequence corresponds to the full length sense gene or only a portion thereof. Further, "an antisense sequence" should read --the antisense sequence--.

At Claim 22, lines 10 and 14, "a nucleotide sequence that corresponds to an antisense sequence" is indefinite. It is unclear if a nucleotide sequence that corresponds to an antisense sequence of another sequence corresponds exactly or not. It is also unclear whether the antisense sequence corresponds to the full length sense gene or only a portion thereof. Further, "an antisense sequence" should read --the antisense sequence--.

Claim 3 recites the limitation "wherein said sequence encodes an invertase inhibitor" in lines 1-2. There is insufficient antecedent basis for this limitation in the claim. In Claim 2b, the sequence recited is antisense and does not encode an invertase inhibitor.

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Claim 5 recites the limitation "the nucleotide sequence encodes an invertase inhibitor" in lines 1-2. There is insufficient antecedent basis for this limitation in the claim. In Claim 2b, the sequence recited is antisense and does not encode an invertase inhibitor.

Claim 12 recites the limitation "the nucleotide sequence encodes an invertase inhibitor" in lines 1-2. There is insufficient antecedent basis for this limitation in the claim. In Claim 11d, the sequence recited is antisense and does not encode an invertase inhibitor.

Claim 4 is confusing in its recitation of "a sequence in a plant cell operably linked to a nucleic acid sequence of Claim 2". It is unclear whether "a sequence" refers to an additional sequence ligated to that of Claim 2, or whether "a sequence in a plant cell" merely refers to the ability of the promoter to function in plants. If the latter were intended, insertion of --plant-functional-- before "promoter", and deletion of "capable of driving expression of a sequence in a plant cell" would obviate this rejection. In addition, "a nucleotide sequence of claim 2" should be replaced with --the nucleotide sequence of claim 2-- to indicate that the entire sequence was intended.

### ***Claim Rejections - 35 USC § 102***

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

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6. Claims 2, 4, 8-11, 15, 16, 19 and 20-22 are rejected under 35 U.S.C. 102(b) as being anticipated by Bussis D. *et al.*, Planta 1997, 202:126-136.

The claims are broadly drawn to a nucleotide sequences of Claims 2(d), 11(g), and 20-22(g) that hybridizes to any sequence of Claim 2(a-c), 11(a-f), and 20-22(a-f) in particular sequences that under low stringency conditions would hybridize to said sequences.

Bussis teaches a transformed dicot overexpressing a yeast polynucleotide coding for an invertase enzyme (Abstract lines 1-9). Thus, the reference discloses the all the limitations of the instant Claims 2, 4, 8-11, 15, 16, 19 and 20-22.

7. Claims 2, 4, 8-11, 14, and 16-22 are rejected under 35 U.S.C. 102(a) as being anticipated by Rausch T. *et al.*, WO 00/09719 A1.

The claims are broadly drawn to a nucleotide sequence that corresponds to an antisense sequence of a polynucleotide sequence encoding a maize plant invertase inhibitor (SEQ ID NO: 1) of Claims 2(b), 11(c), and 20-22(c) that hybridizes under stringent hybridization conditions, encompassing low stringency, to any one of the nucleic acid sequences of Claims 2(a-c), 11(a-f), and 20-22(a-f).

Rausch teaches transgenic plants and plant cells comprising a reduced expression of invertase inhibitors using a cDNA sequence in antisense orientation (see entire Abstract). Thus, the reference discloses the all the limitations of the instant Claims 2, 4, 8-11, 14, and 16-22.

8. Claims 2, 4, 8-11, 14, and 16-22 are rejected under 35 U.S.C. 102(b) as being anticipated by Greiner S. *et al.* Plant Physiology, 1998, Vol. 116, pp. 733-742.

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The claims are broadly drawn to a nucleotide sequence that corresponds to an antisense sequence of a polynucleotide sequence encoding a plant invertase inhibitor of Claims 11(d) and 20-22(d) and a nucleotide sequence that hybridizes to any one of the nucleotide sequences of Claims 2(a-c), 11(a-f), and 20-22(a-f).

Greiner teaches PCR amplification and isolation of a cDNA encoding a tobacco apoplastic invertase inhibitor and hence teaches an antisense sequence of a plant invertase inhibitor (page 736, see Figure 2). Thus, the reference discloses the all the limitations of the instant Claims 2, 4, 8-11, 14, and 16-22.

### ***Claim Rejections - 35 USC § 103***

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

10. Claims 17-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bussis *et al.* Planta 1997, 202:126-136 in view of Gordon-Kamm W. *et al.* The Plant Cell, July 1990, Vol. 2, pp. 603-618.

Applicant claims a nucleotide sequence encoding a yeast invertase and overexpression of said nucleic acid sequence in monocot and maize plants transformed therewith.

The teachings of Bussis are discussed *supra*.

Bussis does not teach a transformed monocot overexpressing a polynucleotide encoding a yeast invertase.

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Gordon-Kamm teaches transformation of maize using a DNA construct having the CaMV35S promoter and NOS terminator for expression of foreign genes in maize (page 614 column 1, lines 5-17).

It would have been obvious at the time of Applicant's invention to modify the invention of Bussis to substitute maize transformation and regeneration of maize transformed with a DNA construct comprising a CaMV35S promoter and a NOS terminator sequence as taught by Gorodn-Kamm in order to obtain expression yeast invertase coding sequences in maize plants and seeds. One of skill in the art would have been motivated by the teachings common in the art that the transformation of maize was generally successful and that one would have had a reasonable expectation of success of regenerating transformed maize plants and seeds.

11. All claims are rejected.

12. Claims 3, 5-7, and 12-13 are deemed free of the prior art, given the failure of the prior art to teach or suggest an isolated polynucleotide of SEQ ID NO: 1 encoding a polypeptide of SEQ ID NO 2, the antisense polynucleotide sequence of SEQ ID NO: 1, plants transformed with said polynucleotides, and a method for increasing the yield in a plant expressing said polynucleotides.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Russell Kallis whose telephone number is (703) 305-5417. The examiner can normally be reached on Monday-Friday 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (703) 306-3218. The fax phone numbers for the Group is (703) 308-4242 or (703) 305-3014.

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Any inquiry of a general nature or relating to the status of this application or proceeding,  
or if the examiner cannot be reached as indicated above, should be directed to the legal analyst,  
Sonya Williams, whose telephone number is (703) 308-0009.

Russell Kallis Ph.D.  
October 16, 2002

DAVID T. FOX  
PRIMARY EXAMINER  
GROUP 180-1638

A handwritten signature in cursive script, appearing to read "David T. Fox", followed by the number "14".